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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/043,787	01/10/2002	Chong-Sheng Yuan	466992000221	9117

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/043,787	YUAN, CHONG-SHENG	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-50* is/are pending in the application.

4a) Of the above claim(s) *36-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8-35* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see attached*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 1-4 and 6-50 are pending.

Applicant's amendment of claims 1, 7-8, 10, 11, 12, 18-22, 26, 28-29, and cancellation of claim 5 in a communication filed on 6/14/2004 is acknowledged.

Applicants request that Groups directed to the non-elected mutants listed in claim 7, i.e. Groups I-XIV, XVI-LXII, be rejoined for examination in the instant application. Applicants argue that it is unclear to Applicants whether it is a restriction requirement or an election of species. Furthermore, Applicants argue that the Examiner did not state why each of Groups I-LXII is able to support separate patents and is independent or distinct. Also, Applicants submit that the Examiner examined the full scope of claim 7.

Applicant's arguments have been fully considered. The restriction requirement mailed on 7/25/2003 never stated that the requirement was an election of species. This is evidenced by the fact that each of the mutants was assigned to a different group, i.e. I-LXII. If an election of species would have been required, an explicit statement indicating that an election of species was required would have been made. Furthermore, contrary to Applicant's assertion, the Examiner clearly indicated why the inventions were distinct. See particularly the sentence prior to paragraph 2 and paragraph 4, where it is stated why each of the mutant proteins recited is distinct. Also, in regard to arguments as to whether each of the Groups I-LXII is able to support separate patents, it is noted that, absent evidence indicating that the mutant polypeptides recited in the method of claim 7 are obvious variations of the polypeptide of SEQ ID NO: 1, the Examiner considers each of the mutant polypeptides an independent and distinct polypeptide. Thus, a method of use of an independent and distinct polypeptide would also be considered an independent and distinct invention. While the inventions of Groups I-LXII have been found to be independent and distinct, a search of the subject matter encompassed by claim 7 has been conducted in

the previous Office Action. Thus, the restriction requirement previously presented of Groups I-LXII is hereby withdrawn.

This application contains claims 36-50 drawn to inventions non-elected without traverse in a communication filed on 11/28/2003. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 6/14/2004 was filed after the mailing date of the Office Action on 2/10/2004. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

2. The information disclosure statement (IDS) submitted on 2/6/2004 is acknowledged. This IDS was not previously considered in view of the fact that it was not available to the Examiner prior to the submission of the previous Office Action. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

3. Applicants request reconsideration of references 65 and 128 of the IDS submitted on 12/30/2002 in view of the evidence submitted. In view of the evidence submitted, references 65 and 128 are being considered by the examiner.

Claim Objections

4. Claim 18 is objected to due to the recitation of "wherein the SAH is contacted with the mutant SAH hydrolase" for the following reasons. While claim 1 refers to a method for assaying Hcy, SAH or adenosine in a sample wherein the sample is contacted with the hydrolase, and wherein the sample contains or is suspected to contain SAH, there is no specific step in claim 1 wherein SAH in the sample is

isolated such that it can be contacted with the hydrolase as recited in claim 18. For clarity and consistency, it is suggested that the claim be amended to recite "wherein the sample is contacted with the mutant ....". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-4, 6-32 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite due to the recitation of "catalytic activity". Applicants argue that the specification in page 12 refers to a mutant SAH hydrolase as one which lacks detectable levels of one of its catalytic activities or its overall catalytic activities compared to its wild-type counterpart. Applicant's arguments have been considered but are not deemed persuasive. However, in view of Applicant's disclosure in page 20, lines 12-15 of what is encompassed by the catalytic activity of the enzyme in the hydrolytic direction, this rejection is hereby withdrawn.

7. Claim 2 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection was applied due to the recitation of the term "amino acid directly involved in the SAH hydrolase's catalytic activity". Applicants argue that the term is clear to one of skill in the art and points the Examiner's attention to page 20, lines 10-24. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. The specification at page 20 does not provide a definition or clarification as to what is encompassed by the term "directly involved" as it relates to catalytic activity. The section of the specification indicated by Applicants refer to 20 amino acids which interact with the substrate inhibitor and co-enzyme NAD+ in the x-ray crystal structure of the human SAH hydrolase in complex with a substrate analog inhibitor, and how one of skill in the art can make

mutations of residues involved in substrate binding and catalysis. Also, it does not indicate if it encompasses both (1) residues which if mutated eliminate catalytic activity, and (2) residues which if mutated may alter catalytic activity (i.e. reduction or increase). For examination purposes, the same interpretation indicated in the previous Office Action will be used. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4, 6, 8-35 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been discussed at length in the previous Office Action mailed on 2/10/2004. It is maintained for the reasons of record and those discussed below.

10. Applicants argue that the claims are now amended such that they recite "a mutant SAH hydrolase derived from a mammalian SAH hydrolase". According to Applicants, the specification teaches a representative number of mutant SAH hydrolases and information correlating structural features with functional characteristics. Applicants submit that the fact that a human and a rat SAH hydrolase are known, their crystal structures determined, and the high level of conservation among SAH hydrolases, the specification provides ample description correlating structure and function. Applicants argue that the Examiner's references previously presented do not support the argument of unpredictability in the SAH hydrolase art. In particular, Applicants submit that the enzymatic activity referred to in the references is

not pertinent to SAH hydrolases. It is Applicant's contention that the Examiner has not established lack of written description.

11. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 1-4, 6, 8-35. The Examiner acknowledges that the claims as amended are limited in the genus of mutant SAH hydrolases used in the claimed method, i.e. mammalian-derived mutant SAH hydrolases. The Examiner also acknowledges the teachings of the art in regard to the crystal structure of the human and rat SAH hydrolases known. However, the Examiner disagrees with Applicant's contention that what is known in the art and what has been disclosed in the specification is sufficient to adequately describe all the species of mutant mammalian SAH hydrolases having the functional characteristics recited in the claims, i.e. binding affinity for Hcy, SAH or adenosine but attenuated catalytic activity. While the mutants described in the specification appear to have the functional characteristics recited in the claims, the specification fails to provide (1) the structural elements common to all mammalian SAH hydrolases, and (2) the specific structural changes which can be made to any mammalian SAH hydrolase such that they display the functional characteristics required. While it appears that several rat, one mouse and two human SAH hydrolases are known, and it is suggested that these enzymes are highly conserved during evolution, it is unclear as to how the disclosure of the structure of these species of the mammalian genus is sufficient to predict the structure of any mammalian SAH hydrolase if nothing is known as to how much structural conservation (i.e. % structural homology) is common among all the members of the genus and which are the structural elements most likely to be conserved. Furthermore, the disclosure of the structure of these species does not provide one of skill in the art with a clue as to which are the structural elements which are most likely to be variable in all the species of the genus and the role of that variability in SAH hydrolase activity or binding affinity. It is noted that in humans alone, it would not be uncommon to find other SAH hydrolases which are not coded by the same gene which encodes the polypeptide of SEQ ID NO: 1. Thus, it is unclear as to how the

disclosure of two human SAH hydrolase would be representative of any human SAH hydrolase, let alone all mammalian SAH hydrolases. Contrary to Applicant's assertion, neither the art nor the specification provide a correlation between structure and function for all the species in the genus. While some of the findings in regard to the structure/function correlation found in regard to the human and rat SAH hydrolases may be applicable to some of the species in the genus, in the absence of additional information regarding the structures of other species in the genus, the level of structural variability among all the species, and the level of structural conservation among all the species, it is unclear as to how one of skill in the art can reasonably conclude that the same correlation would apply to any mammalian SAH hydrolase.

While it is agreed that the art previously cited does not specifically refer to SAH hydrolases, the art was introduced to support the argument that the art teaches several examples of how minimal structural changes, even conservative ones, do have an effect in enzymatic function which was not expected based solely on structural homology. See particularly the teachings of Witkowski et al. and Seffernick et al. Thus, contrary to Applicant's assertions, the art presented by the Examiner provides examples of the unpredictability of the art in regard to assigning function based solely on structural homology. In the absence of any knowledge or guidance as to a structure/function correlation which is applicable to all members of the genus, the disclosure of a few species from human, mouse and rat, is not deemed sufficient to adequately describe the entire mammalian genus.

The genus of polypeptides required to practice the claimed method is a very large genus with the potentiality of being a highly structurally variable genus. While a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus, in the instant case, there is no structural feature which is representative of all the members of the genus of mutant mammalian-derived SAH

hydrolases recited in the claim. Many structurally unrelated polypeptides are encompassed by the genus recited. The specification discloses only a few mutants of a single human placental SAH hydrolase which have the functional characteristics required, i.e. attenuated catalytic activity and binding affinity for Hcy, SAH or adenosine, which is insufficient to adequately describe the required genus of mutant mammalian SAH hydrolases having these specific functional characteristics.

12. Claims 1-4, 6, 8-35 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for assaying Hcy, SAH, or adenosine with a mutant SAH hydrolase, wherein said SAH hydrolase comprises the amino acid sequence set forth in SEQ ID NO: 1 and also comprises the substitutions at those positions recited in claim 7 and those positions disclosed in the specification, wherein said mutant SAH hydrolase has attenuated 3'-oxidative activity, 5'-hydrolytic activity, and/or 3' reduction activity, and the same, or higher, binding affinity for Hcy, SAH or adenosine when compared to the polypeptide of SEQ ID NO: 1, wherein the mutant SAH hydrolase can be labeled and wherein a labeled Ado-Cys or Ado-5'ester can be used, does not reasonably provide enablement for (1) a method for assaying Hcy, SAH, or adenosine using any mammalian-derived mutant SAH hydrolase having the functional characteristics recited in the claims, (2) the method of (1) further comprising detecting cholesterol and/or folic acid in the sample by any means, or (3) the method of (1) further comprising detecting cholesterol and/or folic acid in a sample by any means, wherein the mutant SAH hydrolase comprises SEQ ID NO: 1 and also comprises the amino acid substitutions recited in claim 7 or in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection has been discussed at length in the previous Office Action mailed on 2/10/2004. It is maintained for the reasons of record and those discussed below.

13. Applicants argue that the specification provides ample guidance to practice the claimed invention. Applicants submit that several wild-type SAH hydrolases are known and that the specification provides guidelines to make and select the required mutants. Also, applicants argue that methods of generating mutants and the crystal structure of a human and rat SAH hydrolase are known in the art. According to Applicants, these crystal structures and what is disclosed in the specification should allow one of skill in the art to practice the claimed invention without undue experimentation. It is Applicant's contention that a considerable amount of experimentation is permissible if it is merely routine. Therefore, it is Applicant's opinion that identifying and cloning mammalian SAH hydrolases and generating mutants as required by the claimed method would require routine experimentation. Applicants submit that the references cited by the Examiner do not support the unpredictability of the art for SAH hydrolase. Furthermore, Applicants submit that even in an unpredictable art, Applicants are not required to teach every species encompassed by the claims. Applicants note that the specification does not need to teach what is well known in the art, such as SAH derivatives and analogs or methods to detect cholesterol or folic acid.

14. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. The Examiner acknowledges the teachings of the art in regard to the disclosure of several rat, one mouse and two human SAH hydrolases, SAH hydrolase activity assays, as well as the crystal structures of a human and a rat SAH hydrolase. However, the Examiner disagrees with Applicant's contention that the specification and the teachings of the prior art enable the full scope of the claimed invention. The claims require an extremely large number of mutant SAH hydrolases, i.e. mammalian-derived SAH hydrolases, which display specific functional characteristics, such as a binding affinity for Hcy, SAH or adenosine enhanced 50 times compared to the wild-type counterpart and attenuated catalytic activity. To obtain the genus of mutant SAH required, one of skill in the art would require (1) the structures of all wild-type mammalian SAH hydrolases , and (2) the specific amino acid

residues in all wild-type mammalian SAH hydrolases which can be modified such that the required functional characteristics are display, as well as the amino acid residues which can be used to substitute those found in the wild-type mammalian SAH hydrolases to obtain the mutant SAH hydrolases. The specification provides several mutants of a single mammalian SAH hydrolase, i.e. human placental SAH hydrolase comprising SEQ ID NO: 1, which display the desired characteristics. As indicated above, while some rat, mouse and human SAH hydrolases are known, and it is suggested that there is high conservation in evolution among SAH hydrolases, there is no teaching in the specification or the art regarding the level of structural conservation found among all mammalian SAH hydrolases, i.e. % structural homology, the level of variability, and the effect of that variability in SAH hydrolase activity or binding affinity to Hcy, SAH or adenosine. It is reiterated herein that contrary to Applicant's assertion, neither the art nor the specification provide a correlation between structure and function for all the species in the genus. While some of the findings in regard to the structure/function correlation found in regard to the human and rat SAH hydrolases may be applicable to some of the species in the genus, in the absence of additional information regarding the structures of other species in the genus, the level of structural variability among all the species, the level of structural conservation among all the species, and the structural elements which correlate with increased binding affinity for Hcy, SAH or adenosine and reduced catalytic activity, it is unclear as to how one of skill in the art can reasonably conclude that the same correlation would apply to any mammalian SAH hydrolase.

The Examiner acknowledges that (1) SAH hydrolase assays are known in the art, (2) there is no requirement for disclosing every single species encompassed by a genus, and (3) the specification does not need to teach what is well known in the art. However, in the instant case, what is disclosed in the specification and what is known in the prior art does not prevent undue experimentation. While it is agreed that cloning and isolation of other SAH hydrolases which share some structural homology to those known in the art may not be considered undue experimentation in view of the fact that the hybridization

probes used would have structural elements which correspond to those in known SAH hydrolases, isolation of SAH hydrolases which share very little structural homology to what is known in the art would not be considered routine experimentation. Therefore, contrary to Applicant's assertion, cloning and isolation of any mammalian SAH hydrolase wherein the SAH hydrolase shares very little structural homology with what is known in the prior art would constitute undue experimentation, unless something is known about the structure of what is to be isolated. Furthermore, even if cloning and isolation of any mammalian SAH hydrolase could be done without undue experimentation, the method requires mutants of mammalian SAH hydrolases wherein the mutants display specific functional characteristics. However, neither the specification nor the art teaches those specific structural elements in any mammalian SAH hydrolase which can be mutated to obtain a SAH hydrolase having, for example, at least 50 times enhanced binding affinity for Hcy, SAH or adenosine and attenuated catalytic activity. As mentioned previously, while it is agreed that the teachings of the art previously presented by the Examiner do not specifically address SAH hydrolases, the art presented by the Examiner clearly teaches that even a single amino acid substitution can lead to a change in enzymatic function. Therefore, while not specifically addressing SAH hydrolases, the art introduced by the Examiner clearly teaches examples using different enzymatic activities, where it is shown the unpredictability of assigning function based solely on structural homology as small structural changes can lead to major changes in function.

In regard to arguments that the specification does not need to teach all SAH derivatives and analogs, or methods to detect cholesterol or folic acid, it is noted that it its not clear from the specification if derivatives are different from analogs as used in the claims. There is no definition in the specification indicating whether these terms are intended to be equivalent. If one assumes that the intended meaning of these terms is "compounds which would bind to SAH hydrolase wherein said compounds share structural similarity to SAH", then arguments regarding the genus of SAH derivatives/analogs are found persuasive. In regard to the detection of cholesterol and folic acid, while the Examiner is not arguing that cholesterol

and folic acid detection methods are not known in the art, it is noted that the method of claim 35 requires the use of the same sample used to detect Hcy, SAH or adenosine for detection of cholesterol and/or folic acid. As such, the sample will be treated using any means necessary to detect binding of Hcy, SAH or adenosine before it can be used to detect cholesterol and/or folic acid. According to the specification and the claims, the method may require the addition of reducing agents, SAH hydrolase inhibitors, SAH derivatives/analogs, etc. It is unclear from the teachings of the specification if any of the treatments required in a method to detect Hcy, SAH or adenosine would affect the detection of cholesterol or folic acid using the methods known in the art regarding cholesterol or folic acid. Thus, one cannot reasonably conclude that the same methods known in the art for detection of cholesterol/folic acid would be effective in a sample which has been treated to detect Hcy, SAH or adenosine. Therefore, in view of the teachings of the specification and the teachings of the prior art, one cannot reasonably conclude that the claimed invention is fully enabled by the specification.

Double Patenting

15. Claims 1-3, 6, 8-9, 18-19, 23-24, 30-34 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 6-14, and 16 of U.S. Patent No. 6376210.

16. Applicants submit that they will address the double patenting rejection when allowable subject matter is identified. In view of the fact that no arguments have been presented which point out disagreements with the Examiner's position, no amendments to the claims have been made which change the scope of the claims such that they would overcome the rejection, and no terminal disclaimer has been filed, the instant rejection is maintained for the reasons of record.

Allowable Subject Matter

17. Claim 7 appears to be allowable over the prior art of record but it is objected to as it depends upon a base rejected claim.

Conclusion

18. No claim is in condition for allowance.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

21. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through

Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
September 1, 2004